Danish 3R-Center

RRR

Replacement Reduction Refinement

More than 140 participants. Please use the opportunity for networking. Presentations are covered and with abstracts and selected PDFs of presentations.

**Annual meeting as a 2 day symposium –**

**This year with several European speakers**

## Program 10th November

**News from 3R centres and activities**

DK: European engagement, survey, teaching, 3R prize, grants

NC3R: More than 10 years 20 employed, supported 238 major awards, active interaction with researchers, SMEs, industry Acute tox study with impact on ICH M3 guideline, Data sharing, Arrive, Crack it, ExpDesignerAssistant. Discussion about inclusion of animal welfare organisations

## Program 10th November

**News from 3R centres and activities**

Århus: Symposium on Metaanalysis 16+17. November

Novo Nordic: 4 persons engaged in new 3R unit focusing on internal projects and internal collaborations. First in the world. Established on ethical grounds.

## Program 10th November

**News from 3R centres and activities**

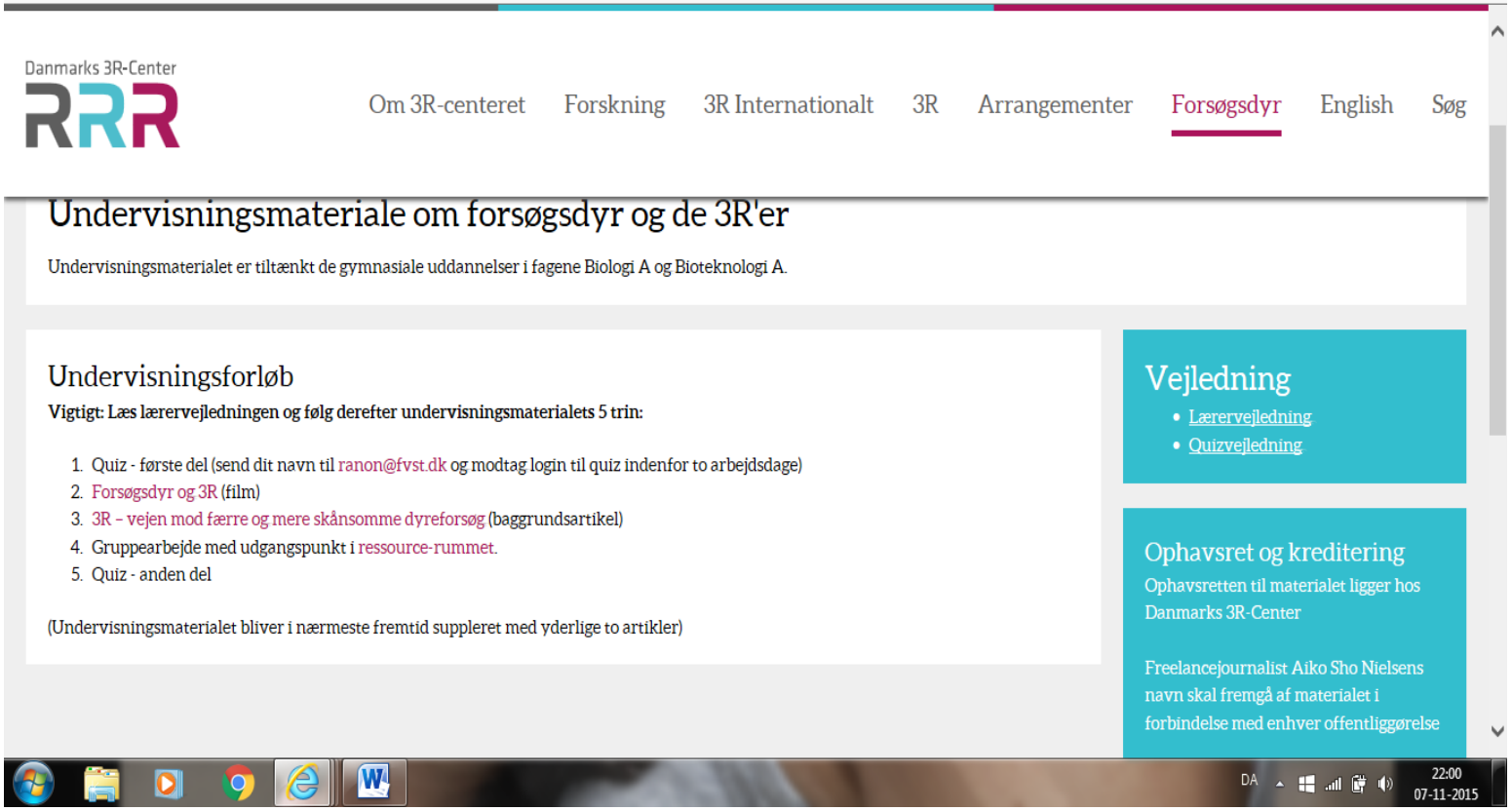
Presentation of last years 3R projects supported by the 3R centre:

Polyclonal antibodies in chicken – Otto Kalliokoski

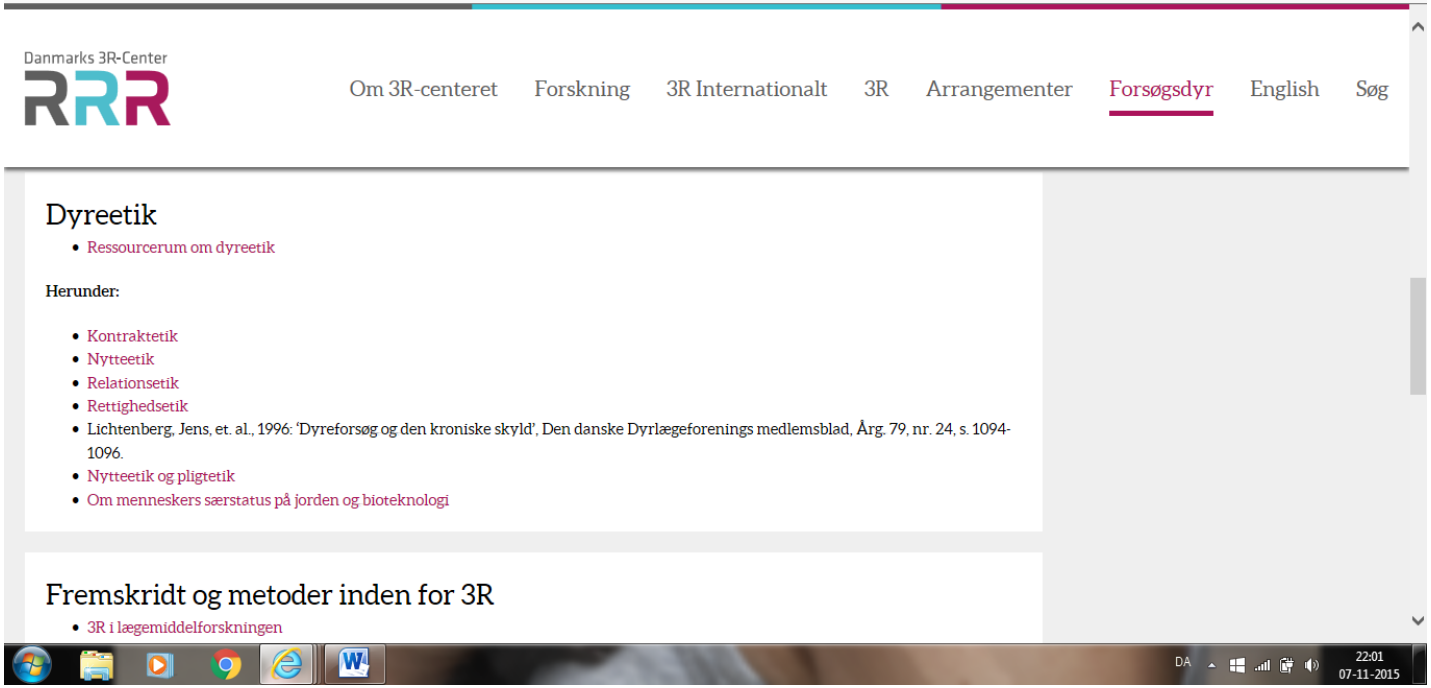
In vitro human skin model – Mette Elena Skindersøe

In vitro model to predict lung toxicity – Søren Thor Larsen

# 'Home'Teaching material for high school from 3R centre



# 'Resource room' – group assignments (detailed and deeper understanding)



# The 3Rs: on animal scientists' perceptions, awareness and practices

**Overall aim:** to improve the basis for further implementation of the 3Rs in Denmark and establish a baseline for assessing future implementation

**Research questions**

1. What is the level of awareness and knowledge about the 3Rs among Danish animal scientists?
2. To what extend are the 3Rs implemented in practice?
3. What are the barriers for further implementation?

# Summing-up the obstacles and opportunities

- Viewed as a whole, most welcome the 3Rs and see no obstacles
- The publicly employed see more obstacles than the privately employed
    - Obstacles are mainly technical/ innovational

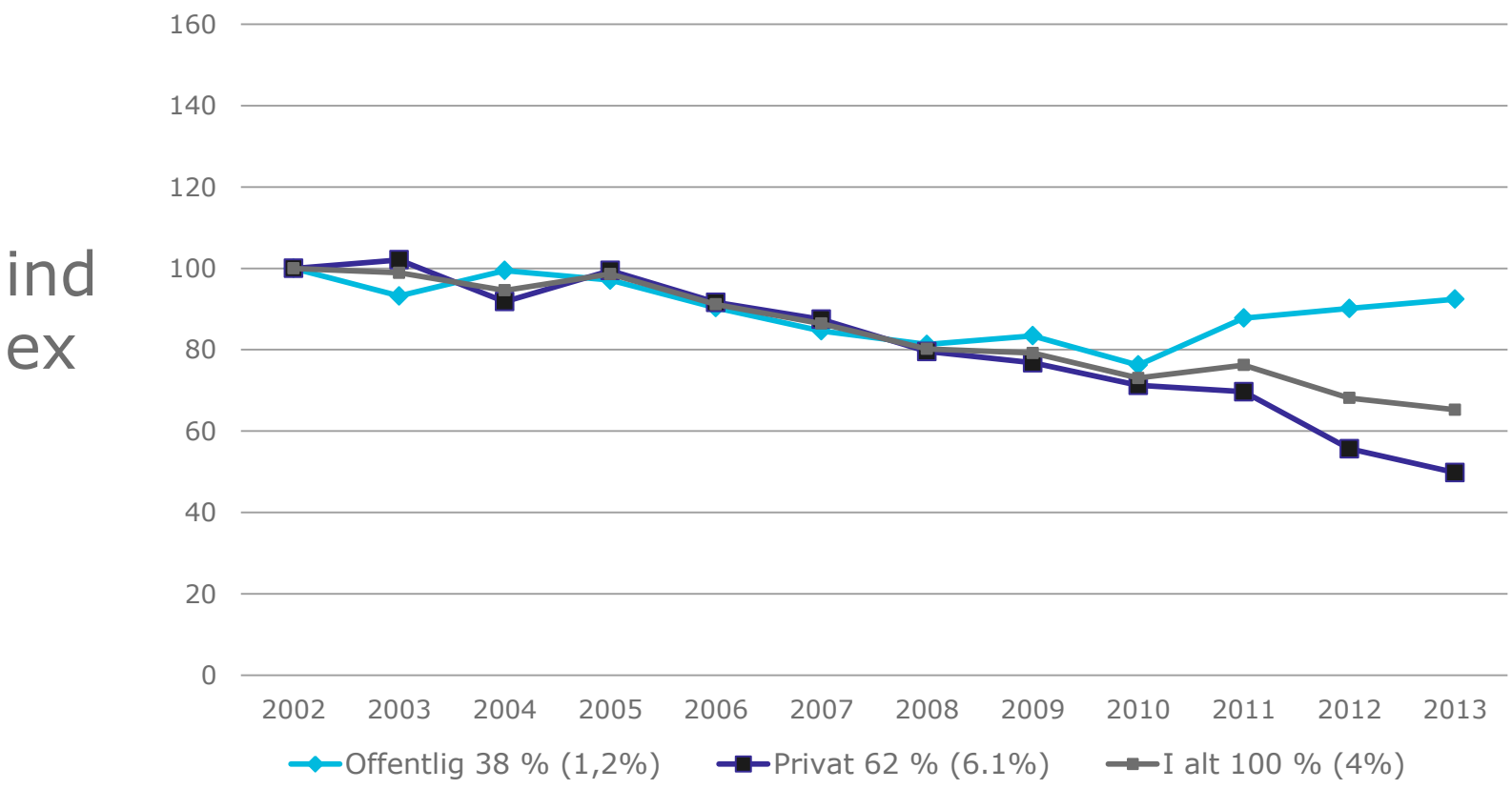
- Increased data sharing is seen as an important means to achieve an overall reduction of the number of animals used

- Replacement generally not considered as feasible as the other Rs and seems to be the greatest challenge
    - progress could be achieved by education

# Preliminary findings

Danish 3R-Center RRR

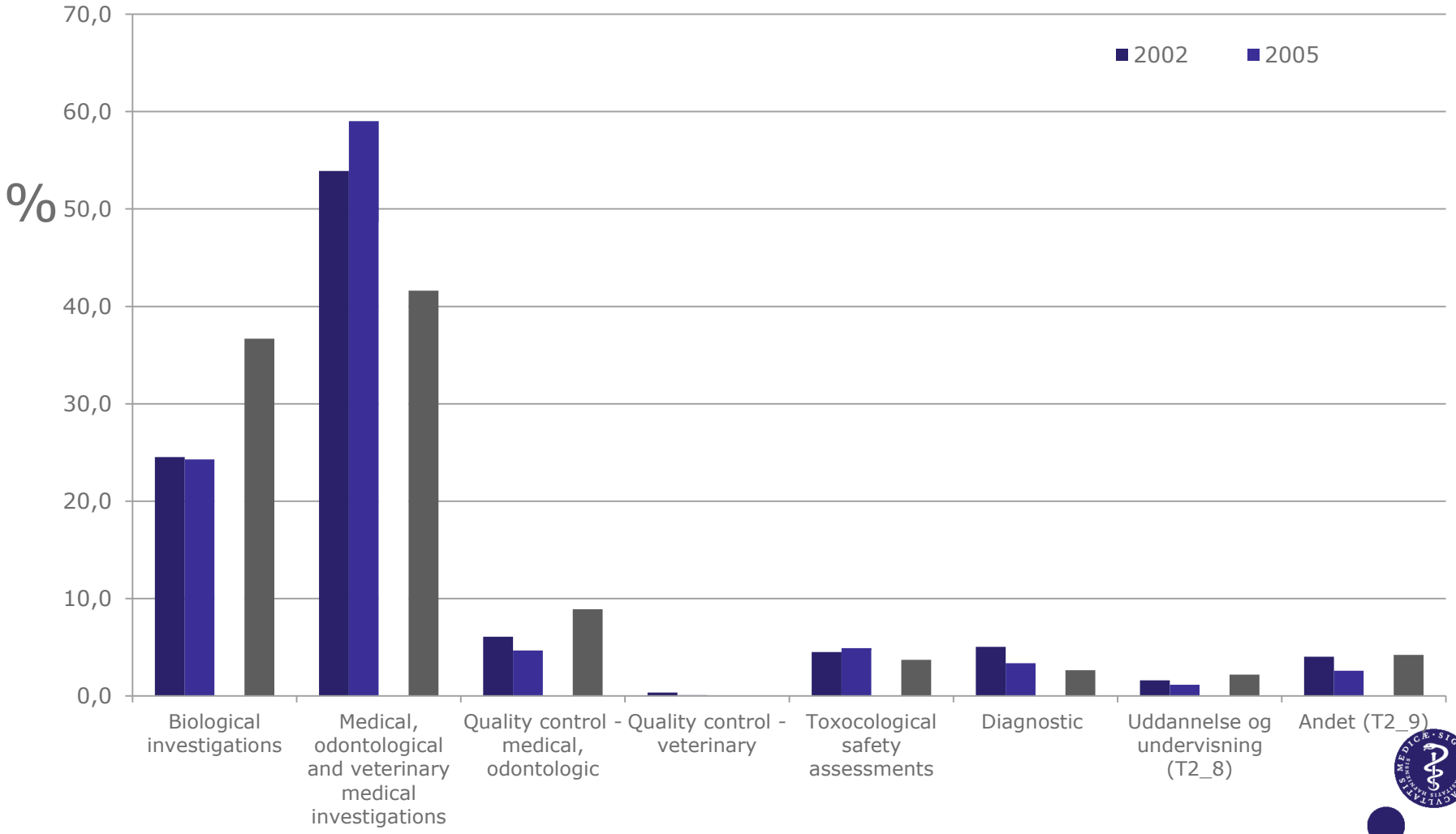
## Number of animals used



# Preliminary findings

Danish 3R-Center RRR

## Types of investigations – selected years



# **Animal use for science in Europe.** Daneshian M, Busquet F, Hartung T, Leist M. ALTEX. 2015;32(4):261-74.

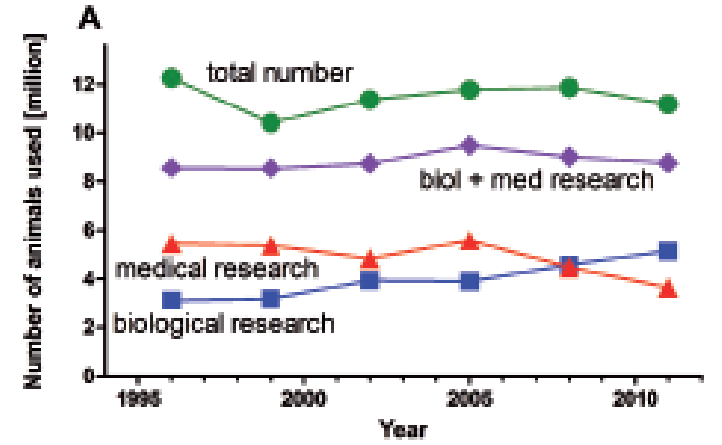



**Fig. 1: Numbers of animals used for scientific purposes in 16 core European countries**

Data obtained from European Commission reports on the statistics on the number of animals used for experimental and other scientific purposes in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Portugal, Spain, Sweden, Switzerland, The Netherlands and United Kingdom for the years 1996, 1999, 2002, 2005, 2008 and 2011; corresponding data from Switzerland were obtained from the Swiss federal food safety and veterinary office; (A) Total number of animals used (green circles), and detail numbers for research and development for medicine, veterinary and dentistry, summarized as medical research (red triangles), biological research, which refers to basic biological research (blue squares) and medical + biological research combined (purple diamonds). (B) The proportion of animals used for the purpose of safety assurance, i.e., toxicological testing (red triangles), for diagnostic (blue squares) and education purposes (green circles).

**Animal use for science in Europe.** Daneshian M, Busquet F, Hartung T, Leist M. ALTEX. 2015;32(4):261-74.

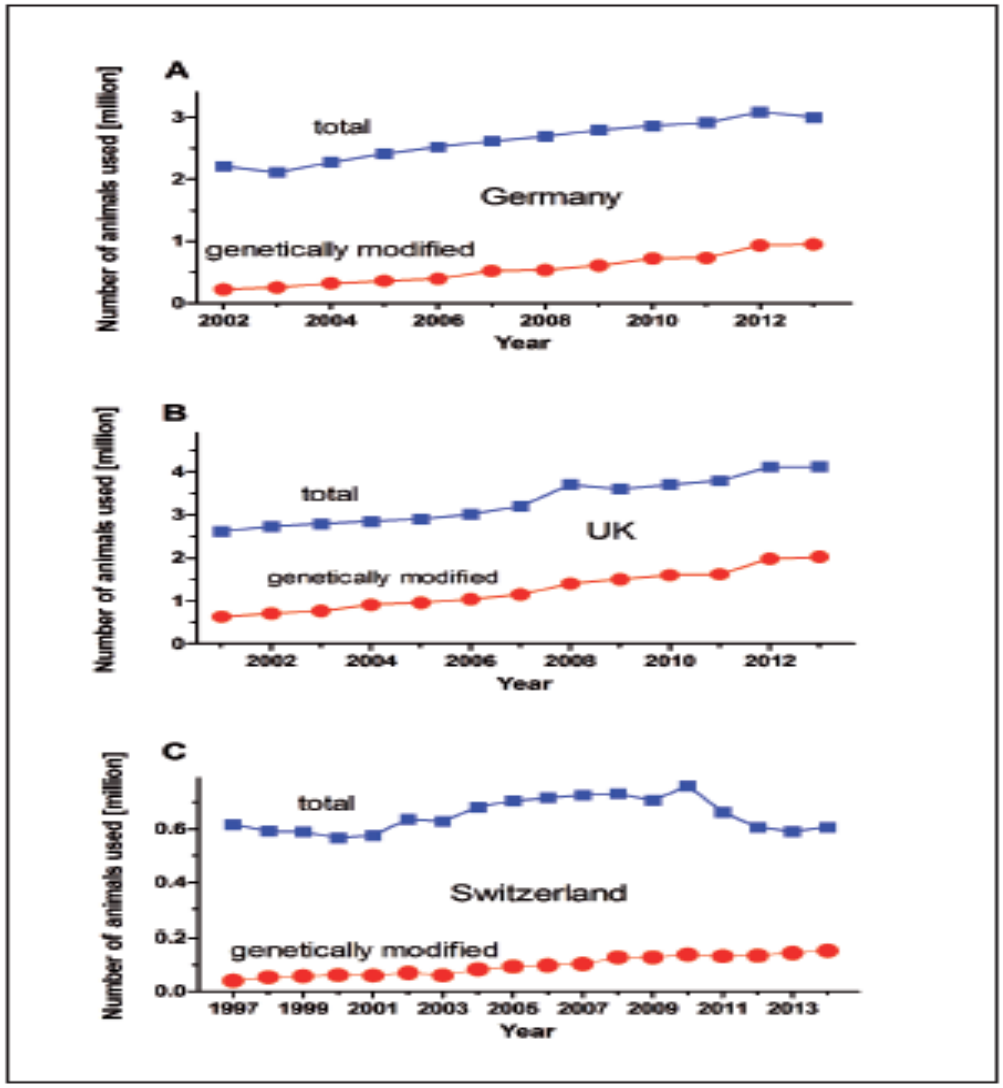



Fig. 2: National examples for the number of transgenic and non-transgenic animals used for scientific purposes

The total annual number of animals (blue squares) and genetically-modified animals (red circles) in (A) Germany, (B) UK and (C) Switzerland. Data are from annual publications on statistics on animals used for scientific purposes from the German Federal Ministry of Food and Agriculture (BMEL), the UK Home Office and the Swiss Federal Food Safety and Veterinary Office (BLV).

**Animal use for science in Europe.** Daneshian M, Busquet F, Hartung T, Leist M. ALTEX. 2015;32(4):261-74.

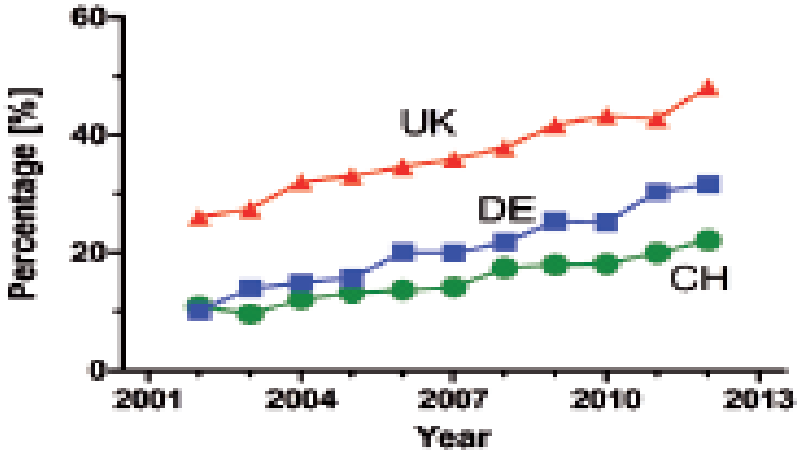



**Fig. 3: Proportion of genetically modified animals of the total number of animals**

The graph shows the annual percentage of transgenic animals of the total animals used for scientific purposes from 2002 to 2012 in the United Kingdom (UK, red triangles), Germany (DE, blue squares) and Switzerland (CH, green circles). Data are calculated from annual publications on statistics on animals used for scientific purposes from the German Federal Ministry of Food and Agriculture (BMEL), the UK Home Office and the Swiss Federal Food Safety and Veterinary Office (BLV).

# Posters presented

Al-Malahmeh et al, Wagening University: Physiologically based kinetic modelling of bioactivation of myristirum facilitating risk assessment

Yishi Huang et al, Dansih Nanosafe Centre: The constrained drop surfactometer as a toll for toxicological assessment of impregnation spray products

Alayjlouni AM et al, Wagening: Mode of action based risk assessment of the botanical food-borne alkenylbenzene apiol from parsley using physiologically based kinetic (PBK) modelling and read across to safrole

Animals used for scientific purposes
Legislation and implementation
The "Three Rs" and alternative approaches
Replacement, Reduction and Refinement – the "Three Rs"
Validation, acceptance and use
EU activities to advance alternatives
Member State activities to advance alternatives
Finding and distributing information on alternatives
Key resources
Search Tools
Databases
Portals and web-sites
Journals
Other resources and organisations

# Animals used for scientific purposes

## Search Tools

- **EURL ECVAM Search Guide (the Guide)** – The Guide is particularly helpful to inexperienced database users. It represents a useful resource where comprehensive searches for alternatives are required as part of authorisation processes for animal experiments and where regulatory requirements mandate the application of the Three Rs. The Guide provides examples of search procedures and user guidance to facilitate the location of the desired information on Three Rs alternatives; it also includes an inventory of relevant resources, contains a check list (the seven golden steps) to allow for searches in a structured and systematic manner, moreover, search principles, suggested search terms etc. Free copies of the handbook or a pdf version are available from the EU Bookshop.
- **Go3R** - is a free of charge 'semantic' search engine making use of underlying expert knowledge on 3Rs methods to s…ically retrieve Three Rs-relevant information. Currently, the semantic Go3R tool searches in the databases …bMed and TOXNET. Additionally, Go3R allows searching the entire World Wide Web using a Google search with automatic higher ranking of 3Rs relevant websites. Results of PubMed and TOXNET searches are presented to the user together with a dynamic table of contents highlighting 3Rs information and allowing to quickly restrict vast sea… results to relevant documents. The Go3R expert knowledge covers the entire scientific domain of …ernatives to animal testing in all biomedical disciplines, but has a special focus on regulatory toxicity testing.
- **Search.norecopa.no** is a search engine for Norecopa's four **databases**: **3R Guide**, **NORINA**, **TextBase** and **Classic AVs**. The search engine takes into consideration the words which have been entered by the user; an index of all the words in the databases; a list of synonyms constructed specifically for these databases; an "auto-complete" function which suggests search terms based on the search engine's own dictionary; algorithms which prioritise or sup…ss words depending on their relevance; Boolean operators, which the user can edit and "fuzzy logic" …words resembling those entered by the user). The user can limit the search to one or more of Norecopa's four databases, or to one or more of a variety of search fields and scientific disciplines.

Last updated: 26/10/2015 | Top


European Commission
Caring for animals
aiming for better science
DIRECTIVE 2010/63/EU
ON PROTECTION OF ANIMALS USED
FOR SCIENTIFIC PURPOSES
ANIMAL WELFARE BODIES AND
NATIONAL COMMITTEES
Environment


European Commission
Caring for animals
aiming for better science
DIRECTIVE 2010/63/EU
ON PROTECTION OF ANIMALS USED
FOR SCIENTIFIC PURPOSES
SEVERITY ASSESSMENT
FRAMEWORK
Environment

# However..

"Simply meeting the legislate requirements will **not** ensure appropriate welfare, care and use practices"

Requires **commitment**

Commitment enabled through **institutional support**

Institutional support facilitated via **regulatory support**

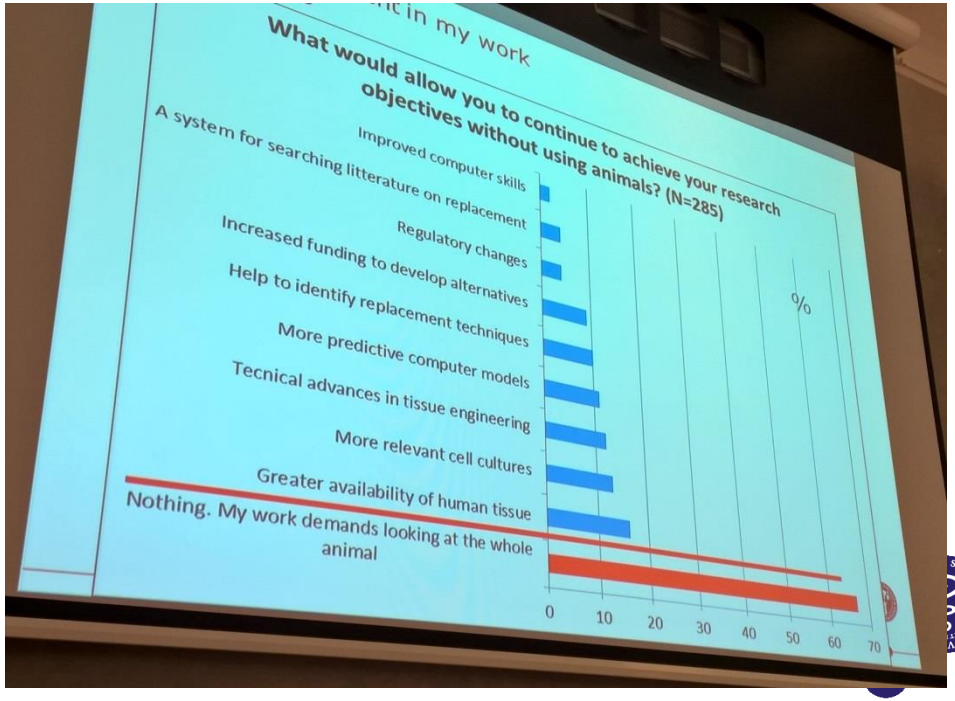
# Culture of Challenge

*Challenge – the path for discovery*

*Researcher*

- **Right questions?**
- **Right disciplines?**
- **Right models?**
- **Beyond obvious?**

- **Refinement..**



## Conclusions

Legal framework, partners and networks in place to strive strategically for new alternative approaches – **take part**

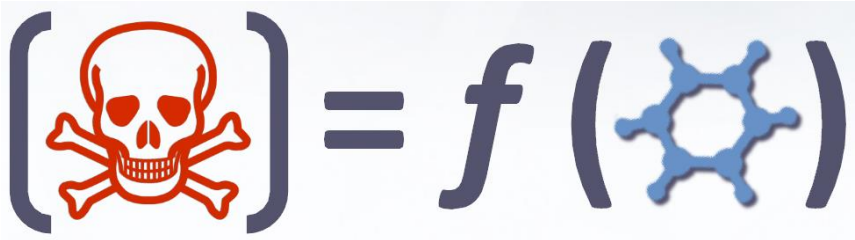
From aspiration to practical, continued implementation of the Three Rs

Three Rs is **everyone's responsibility**

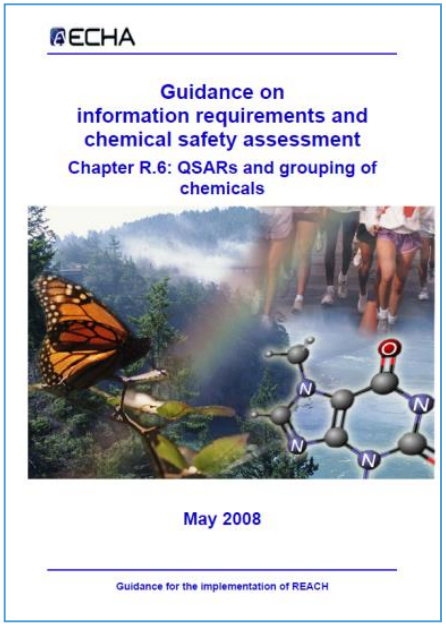
Time to roll out **Culture of Challenge**
- for the benefit of science and animals

# Definition of QSAR: Quantitative Structure-Activity Relationship

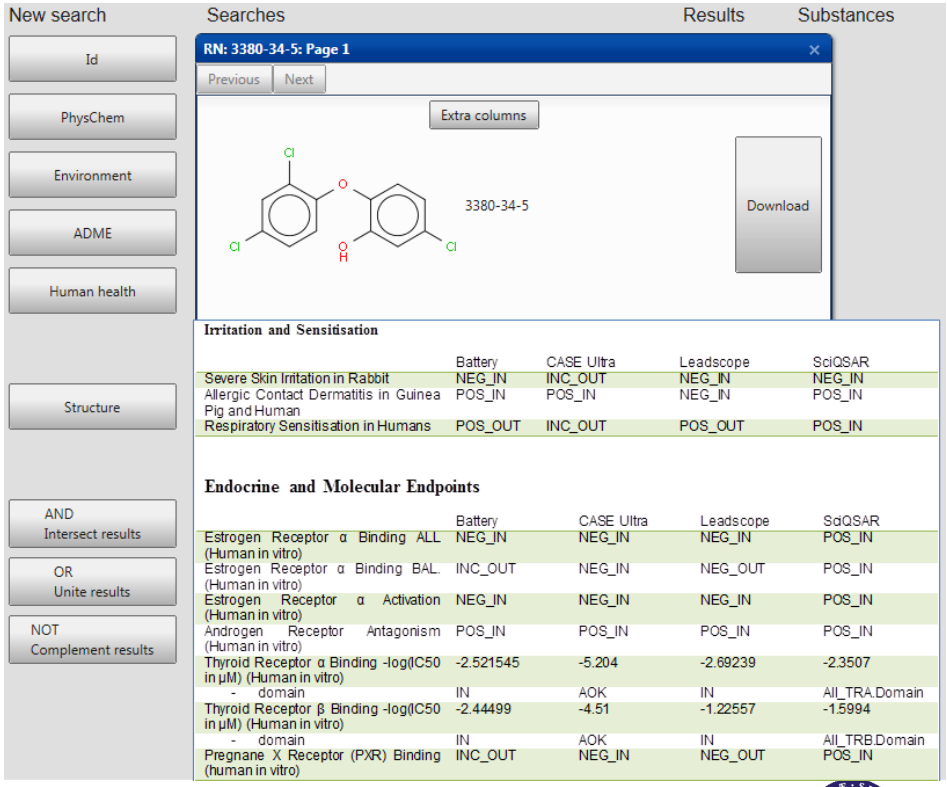
**A QSAR is a mathematical model** (often a statistical correlation) relating one or more parameters derived from chemical structure to a property or activity, e.g. a toxicological endpoint



See e.g. **EU chemicals legislation, REACH, guidance R.6**: "QSARs and grouping of chemicals" for more information
http://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf



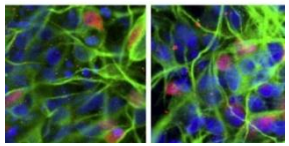
# New Danish QSAR predictions database

# Stem cells as tools to address the 3Rs

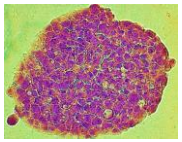
**Stem cells** → **Animal models**

Simple in vitro assays

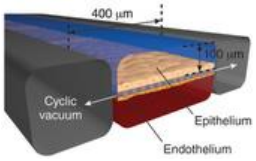


Microfludic systems

Organoids/3D models



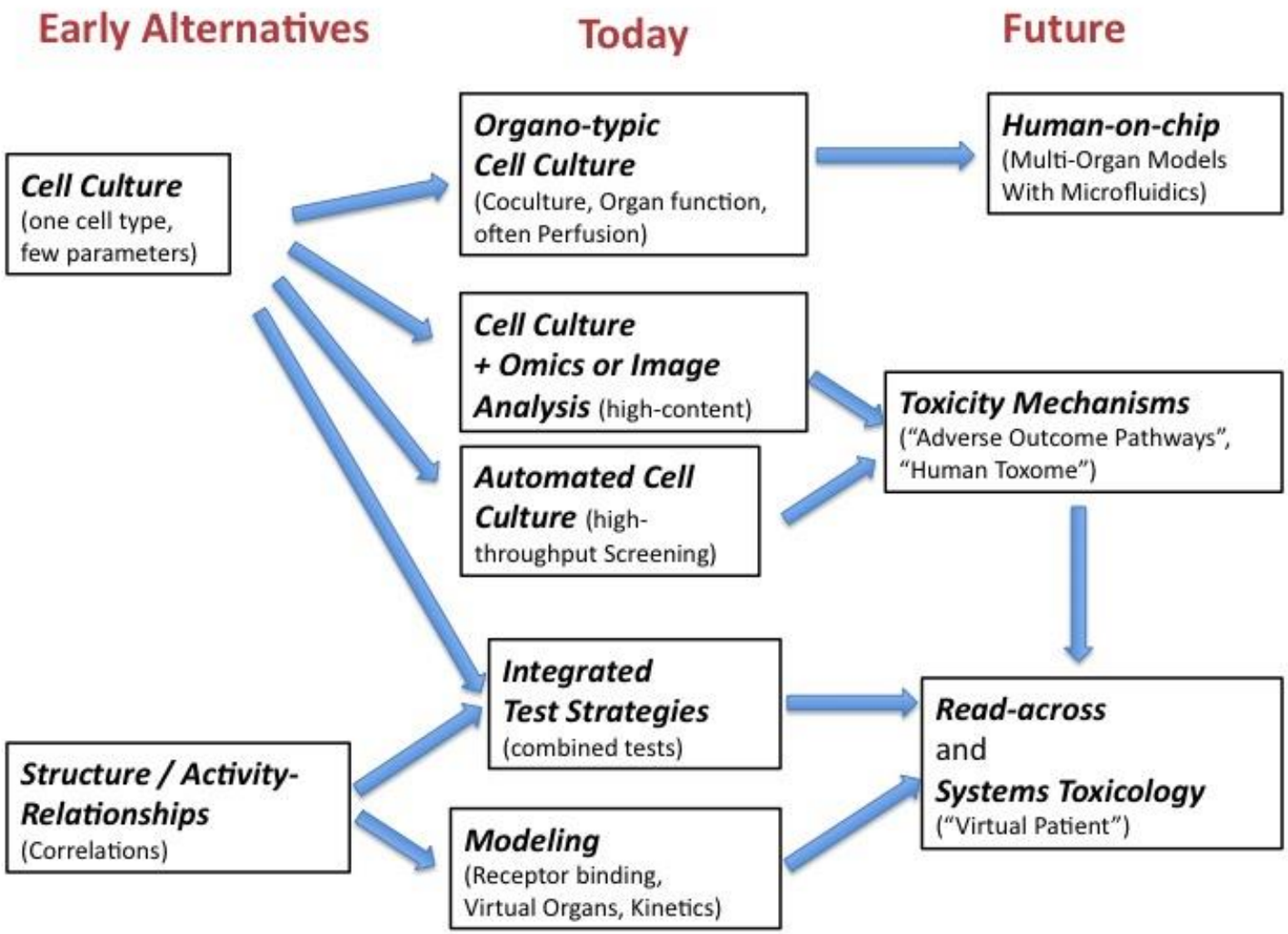
Organs-on-chip




Whole organ models

**Complexity**

DASCS




**CAAT 2.1 – a vision and a strategy**
led by Thomas Hartung

# Hannes remarks

Awareness internally and externally of lab animals welfare through education, communication and dialogie

Review of a lot of applications for permits and of protocols of animal experimentation

Stop for the use of many thousands of mice, rats, rabbits for batch control of efficacy and purity of insulins glucagons, growth hrne and FVII

Stop for use of thousands of mice for production of monoclonal antibodies by the ascites method

Inroduction and use of better anestesia and analgesia

Improvement of housing and environmental enrichment

My 1 priority as lab animal vet has been to be available for the animals, the animal technicians and the scientists

# Announcement of Workshops 14-18 August 2016 at Panum, University of Copenhagen with 3R

**Bridging genomics, human environmental health risk assessment and the 3Rs in animal science**

to be organized by the Nordic Environmental Mutagen Societies (NordEMS) and adhered to program of the European Environmental Mutagen Societies (EEMS), and European Concensus Platform of Alternatives (ECOPA) in August 2016 in Copenhagen.

**Organising committee:**Lisbeth E. Knudsen, University of Copenhagen, Denmark (chair)

Jørn A. Holme, Norwegian Institute of Public Health, Head of Norwegian Society of Pharmacology and Toxicology (NSFT)

Margareta Törnqvist, Stockholm University, Sweden

Tuula Heinonen, president of FICAM and SSCT, Finland

Kristín Ólafsdóttir, University of Iceland